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L1 84 DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 28 DUP REM L1 (56 DUPLICATES REMOVED)

=> s dimerization (p) domain (p) nuclear (p) receptor (p) fusion (p) chimera

L3 12 DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION (P)
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L4 3 DUP REM L3 (9 DUPLICATES REMOVED)

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L5 40 DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) CHIMERA

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L1 84 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION

L2 28 DUP REM L1 (56 DUPLICATES REMOVED)

L3 12 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION (

L4 3 DUP REM L3 (9 DUPLICATES REMOVED)

L5 40 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) CHIMERA

L6 10 DUP REM L5 (30 DUPLICATES REMOVED)

=> d l2 total ibib kwic

L2 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:576800 CAPLUS

TITLE: Oligomerization-Dependent Changes in the Thermodynamic

AUTHOR(S): Properties of the TPR-MET Receptor Tyrosine Kinase
 Hays, John L.; Watowich, Stanley J.
 CORPORATE SOURCE: Department of Human Biological Chemistry and Genetics
 and Sealy Center for Structural Biology, University of
 Texas Medical Branch, Galveston, TX, 77555-0645, USA
 SOURCE: Biochemistry (2004), 43(32), 10570-10578
 CODEN: BICHAW; ISSN: 0006-2960
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Although oligomerization of **receptor** tyrosine kinases (RTKs) is
 necessary for **receptor** activation and signaling, a quant.
 understanding of how oligomerization mediates these critical processes does
 not exist. We present a comparative thermodyn. anal. of functionally
 active dimeric and functionally inactive monomeric soluble analogs of the
 c-MET RTK, which clearly reveal that oligomerization regulates the binding
 affinity and binding kinetics of the kinase toward ATP and tyrosine-containing
 peptide substrates. Thermodyn. binding data for oligomeric c-MET were
 obtained from the dimeric TPR-MET oncoprotein, a functionally active
fusion derivative of the c-MET RTK. This naturally occurring
 oncoprotein contains the cytoplasmic **domain** of c-MET fused to a
 coiled coil **dimerization domain** from the
nuclear pore complex. Comparative data were obtained from a soluble
 monomeric kinase comprising the c-MET cytoplasmic **domain**
 (cytoMET). Significantly, under equilibrium binding conditions, the oligomeric
 phosphorylated kinase showed a significantly lower dissociation constant
 (K_d , dimer = 11 μ M) for a tyrosine-containing peptide derived from the
 C-terminal tail of the c-MET RTK when compared to the phosphorylated
 monomeric kinase cytoMET (K_d , monomer = 140 μ M). Surprisingly, equilibrium
 dissociation consts. measured for the kinase and ATP were independent of the
 oligomerization state of the kinase (.apprx.10 μ M). Stopped-flow anal.
 of peptide substrate binding showed that the association rate consts. (k_2)
 differed 2-fold and dissociation rate consts. (k_{-2}) differed 10-fold when
 phosphorylated TPR-MET was compared to phosphorylated cytoMET. ATP
 binding abrogated the differences in k_2 rates observed between the two
 oligomeric states of the c-MET cytoplasmic **domain**. These
 results clearly imply that oligomerization induces important thermodyn. and
 conformational changes in the substrate binding regions of the c-MET
 protein and provide quant. mechanistic insights into the necessary role of
 oligomerization in RTK activation.

L2 ANSWER 2 OF 28 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 2004277669 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15178411
 TITLE: Controlled transcriptional regulation in eukaryotes by a
 novel transcription factor derived from Escherichia coli
 purine repressor.
 AUTHOR: Yeon Eun-Hee; Noh Ju-Young; Kim Jong-Min; Lee Min-Young;
 Yoon Sarah; Park Sang-Kyu; Choi Kang-Yell; Kim Kyung-Sup
 CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Institute
 of Genetic Science, Yonsei University, College of Medicine,
 134 Shinchon-dong, Seodaemun-gu, Seoul 120-752, Republic of
 Korea.
 SOURCE: Biochemical and biophysical research communications, (2004
 Jun 25) 319 (2) 334-41.
 Journal code: 0372516. ISSN: 0006-291X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200407
 ENTRY DATE: Entered STN: 20040606

Last Updated on STN: 20040721

Entered Medline: 20040720

AB Unlike the DNA-binding **domains** (DBD) of most eukaryotic transcription factors, Escherichia coli LacI family transcription factors are unable to bind to specific target DNA sequences without a cofactor-binding **domain**. In the present study, we reconstructed a novel DBD designated as PurHG, which binds constitutively to a 16bp purine repressor operator, by **fusion** of the purine repressor (PurR) DBD (residues 1-57) and the GAL4 **dimerization domain** (DD, residues 42-148). Binding of PurHG to DNA requires the **dimerization** and a hinge helix of PurR DBD. When the PurHG was expressed as a **fusion** protein in a form of a transcription activator (PurAD) or an artificial **nuclear receptor** (PurAPR or PurAER) responding to ligand, such as RU486 or beta-estradiol, it could regulate the expression of the reporter genes. . . residues from 42 to 75 were sufficient for ligand-dependent regulation in the form of PurAPR. These results suggest that the **dimerization** function of the progesterone ligand-binding **domain** could be substituted for region 76-98 of the GAL4 DD. In summary, the **fusion** of the PurR DBD and the GAL4 DD generates fully active DNA-binding protein, PurHG, in vitro and in vivo, and. . .

L2 ANSWER 3 OF 28

MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2003073778 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12584566

TITLE: Essential role for the dimerization domain of NuMA-RARalpha in its oncogenic activities and localization to NuMA sites within the nucleus.

AUTHOR: Dong Shuo; Qiu Jihui; Stenoien David L; Brinkley William R; Mancini Michael A; Tweardy David J

CORPORATE SOURCE: Section of Infectious Disease, Department of Medicine, Baylor College of Medicine, Houston, TX 77030, USA.

SOURCE: Oncogene, (2003 Feb 13) 22 (6) 858-68.
Journal code: 8711562. ISSN: 0950-9232.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 20030214

Last Updated on STN: 20030304

Entered Medline: 20030303

AB **Nuclear** mitotic apparatus protein-retinoic acid **receptor** alpha (NuMA-RARalpha) is the fourth of five **fusion** proteins identified in acute promyelocytic leukemia (APL) patients. The molecular basis for its oncogenic activity has not been delineated. In. . . M and became associated with the coactivator TRAM-1 at 10(-8) M ATRA. Studies comparing NuMA-RARalpha with NuMA-RARalpha(deltaCC) demonstrated that the **dimerization** or alpha-helical coiled-coil **domain** of NuMA was required for homodimer formation, transcriptional repression of wild-type RARalpha, transcriptional activation of STAT3, and stability of the. . . (YFP)-NuMA. In contrast, CFP-NuMA-RARalpha(deltaCC) exhibited a diffuse granular pattern within the nucleus, similar to RARalpha. These results indicate that the **dimerization domain** of NuMA-RARalpha is critical for each of the known oncogenic activities of NuMA **fusion** proteins as well as its sequestration to **nuclear** sites normally occupied by NuMA and is distinct from RARalpha.

L2 ANSWER 4 OF 28

BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2004:151275 BIOSIS

DOCUMENT NUMBER: PREV200400147492

TITLE: The integrity of the charged pocket in the BTB/POZ-domain is essential for the leukemic phenotype induced by the

AUTHOR(S): APL-associated t(11;17) translocation product PLZF/RAR. Seshire, Anita [Reprint Author]; Zheng, Xiaomin [Reprint Author]; Brambilla, Daria; Ottmann, Oliver G. [Reprint Author]; Hoelzer, Dieter [Reprint Author]; Nervi, Clara; Puccetti, Elena [Reprint Author]; Ruthardt, Martin [Reprint Author]

CORPORATE SOURCE: Med. Klinik III/Haematologie, Klinikum der J. W. Goethe Universitaet, Frankfurt, Germany

SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 589a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB. . . t(11;17) are responsible for the induction of the leukemic phenotype. Both translocations involve the same parts of the retinoic acid **receptor** (RAR) and the PML or PLZF **nuclear** proteins. Both APL **fusion** proteins form high molecular weight complexes (HMW) by oligomerization and aberrantly bind the histone deacetylase recruiting-**nuclear** co-repressor complex (co-repressors). In wild-type (wt) PLZF the BTB/POZ-**domain** is indispensable for its capacity to form HMW. Several point mutations in the BTB/POZ **domain** such as R49D, Y88A and L103E abolish the oligomerization of PLZF, and symmetry-related residues from each of the POZ monomers. . . residues are replaced by neutral, polar residues, still dimerize but is unable to bind to co-repressors. Also in the PLZF/RAR **fusion** protein oligomerization is mediated by the N-terminal BTB/POZ **domain**. In this work we tried to disclose the role of **dimerization** separately from that of the co-repressor binding for the PLZF/RAR-related leukemic phenotype. Hence we studied the effect of the mutations. . . increased significantly the colony formation capacity of Scf+/lin- cells and their self renewal; ii) the mutations R49D and Y88A inhibited **dimerization** not only of PLZF but also of PLZF/RAR, whereas the double mutation D35N-R49Q still allowed to PLZF/RAR to dimerize; iii) PLZF/RAR related block of G/GM-CSF-induced differentiation requires both **dimerization** as well as an intact charged pocket for the binding to the co-repressors; iv) the point mutations (R49D, Y88A, L103E) which interferes with **dimerization**, and the double mutation D35N-R49Q, which interferes in PLZF with the binding to co-repressors, reduced the self renewal of PLZF/RAR positive stem cells to control levels. Taken together these data show that the simple **dimerization** of PLZF/RAR is not enough for the maintenance of the PLZF/RAR-induced phenotype. In fact the formation of a functional charged. . . essential for binding to co-repressors, seems to be indispensable for the PLZF/RAR-induced leukemogenesis. These data establish the charged pocket in BTB/POZ-**domains** of oncogenic proteins such as PLZF/RAR or BCL-6 as a major target for molecular new approaches of molecular therapy.

L2 ANSWER 5 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2004:200342 BIOSIS

DOCUMENT NUMBER: PREV200400200901

TITLE: Analysis of estrogen receptor splice variants responsible for neuroprotection.

AUTHOR(S): Wang, J. [Reprint Author]; Brinton, R. D.

CORPORATE SOURCE: Dept. Mol. Pharmacol. and Toxicology, Sch. of Pharm., USC, Los Angeles, CA, USA

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary

Planner, (2003) Vol. 2003, pp. Abstract No. 504.16.
http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of
Neuroscience. New Orleans, LA, USA. November 08-12, 2003.
Society of Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Apr 2004

Last Updated on STN: 14 Apr 2004

AB. . . via activation of indirect genomic signaling cascades. Recent reports have demonstrated a number of RNA splicing variants for both estrogen **receptor** alpha and beta. We seek to determine whether splice variants of the ER are expressed in neurons and whether one. . . to E2-induced neuroprotection. Analysis of the amino acid structure of these splice variants, indicate variants with a truncated DNA binding **domain** in which the second zinc finger and the **dimerization domain** are deleted. In addition, the **nuclear** translocation **domain** is also deleted. In contrast, a splice variant of the ERbeta contains an additional 18 amino acid insert at the ligand binding **domain**. Based on these analyses, we propose that these particular variants of ER may play a prominent role in mediating the. . . signaling cascades by estrogen. For this purpose, we constructed an ER splice variants and Clontech eGFP-C3 vector to create ER-GFP **fusion** proteins. The ER splice variant-GFP **fusion** protein will be used to determine the dynamics of the individual **receptor** splicing variant in HT-22 cells and rat hippocampal cells in primary culture. Using an overexpression and visible ER model system,. . .

L2 ANSWER 6 OF 28 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2002424540 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12180985

TITLE: Domains of ERRgamma that mediate homodimerization and interaction with factors stimulating DNA binding.

AUTHOR: Hentschke Moritz; Susens Ute; Borgmeyer Uwe

CORPORATE SOURCE: Zentrum fur Molekulare Neurobiologie Hamburg (ZMNH),
Universitat Hamburg, Germany.

SOURCE: European journal of biochemistry / FEBS, (2002 Aug) 269
(16) 4086-97.

Journal code: 0107600. ISSN: 0014-2956.

PUB. COUNTRY: Germany; Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020816

Last Updated on STN: 20021011

Entered Medline: 20021010

AB The estrogen **receptor**-related **receptor** gamma (ERRgamma/ERR3/NR3B3) is an orphan member of the **nuclear receptor** superfamily closely related to the estrogen **receptors**. To explore the DNA binding characteristics, the protein-DNA interaction was studied in electrophoretic mobility shift assays (EMSAs). In vitro translated ERRgamma binds as a homodimer to direct repeats (DR) without spacing of the **nuclear receptor** half-site 5'-AGGTCA-3' (DR-0), to extended half-sites, and to the inverted estrogen response element. Using ERRgamma deletion constructs, binding was found to be dependent on the presence of sequences in the ligand binding **domain** (LBD). A far-Western analysis revealed that ERRgamma forms dimers even in the absence of DNA. Two elements, located in the hinge region and in the LBD, respectively, are necessary for DNA-independent **dimerization**. DNA binding of bacterial expressed ERRgamma requires additional factors present in the

serum and in cellular extracts. **Fusion** proteins of the germ cell **nuclear** factor (GCNF/NR6A1) with ERRgamma showed that the characteristic feature to be stimulated by additional factors can be transferred to a. . .

L2 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:380609 CAPLUS
DOCUMENT NUMBER: 135:805
TITLE: Chimeric proteins containing hormone receptor functional entities and methods of their use
INVENTOR(S): Gage, Fred H.; Suhr, Steven T.; Gil, Elad B.; Senut, Marie-Claude C.
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036447	A2	20010525	WO 2000-US41224	20001017
WO 2001036447	A3	20020815		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001041341	A5	20010530	AU 2001-41341	20001017
EP 1272844	A2	20030108	EP 2000-992120	20001017
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			

PRIORITY APPLN. INFO.: US 1999-421971 A1 19991020
WO 2000-US41224 W 20001017

AB The invention provides chimeric proteins having at least two functional protein units, each containing the **dimerization domain** of a member of the steroid/thyroid hormone **nuclear receptor** superfamily. The chimeric proteins can fold under crystallization conditions to

form functional entities. The functional entities optionally contain a novel flexible peptide linker of variable lengths between at least two of the protein units. In a preferred embodiment, the linker is designed to be increased in increments of 12 amino acids each to aid in preparation of variant chimeric proteins. The DNA binding characteristics of the invention functional entities differ from those of wild-type complexes formed between "monomeric" **receptors** and their binding partners. Some functional entities, e.g. dimers expressed as **fusion** proteins, transactivate responsive promoters in a manner similar to wild-type complexes, while others do not promote transactivation and function instead essentially as constitutive repressors. The invention further provides nucleotide sequences encoding the invention chimeric proteins, cells containing such nucleotide sequences, and methods for using the invention chimeric proteins to modulate expression of one or more exogenous genes in a subject organism. In addition, isolated protein crystals suitable for x-ray diffraction anal. and methods for obtaining putative ligands for the invention chimeric proteins are provided.

L2 ANSWER 8 OF 28 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001667759 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11713274
 TITLE: Domain structure of the NRIF3 family of coregulators suggests potential dual roles in transcriptional regulation.
 AUTHOR: Li D; Wang F; Samuels H H
 CORPORATE SOURCE: Department of Pharmacology, Division of Clinical and Molecular Endocrinology, New York University School of Medicine, 550 First Ave., New York, NY 10016, USA.
 CONTRACT NUMBER: CA16087 (NCI)
 DK09581 (NIDDK)
 DK16636 (NIDDK)
 SOURCE: Molecular and cellular biology, (2001 Dec) 21 (24) 8371-84.
 Journal code: 8109087. ISSN: 0270-7306.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200112
 ENTRY DATE: Entered STN: 20011120
 Last Updated on STN: 20020123
 Entered Medline: 20011221

AB The identification of a novel coregulator for **nuclear** hormone **receptors**, designated NRIF3, was recently reported (D. Li et al., Mol. Cell. Biol. 19:7191-7202, 1999). Unlike most known coactivators, NRIF3 exhibits a distinct **receptor** specificity in interacting with and potentiating the activity of only TRs and RXRs but not other examined **nuclear receptors**. However, the molecular basis underlying such specificity is unclear. In this report, we extended our study of NRIF3-**receptor** interactions. Our results suggest a bivalent interaction model, where a single NRIF3 molecule utilizes both the C-terminal LXXIL (**receptor-interacting domain 1** [RID1]) and the N-terminal LXXLL (RID2) modules to cooperatively interact with TR or RXR (presumably a **receptor** dimer), with the spacing between RID1 and RID2 playing an important role in influencing the affinity of the interactions. During the course of these studies, we also uncovered an NRIF3-NRIF3 interaction **domain**. Deletion and mutagenesis analyses mapped the **dimerization domain** to a region in the middle of NRIF3 (residues 84 to 112), which is predicted to form a coiled-coil structure and contains a putative leucine zipper-like motif. By using Gal4 **fusion** constructs, we identified an autonomous transactivation **domain** (AD1) at the C terminus of NRIF3. Somewhat surprisingly, full-length NRIF3 fused to the DNA-binding **domain** of Gal4 was found to repress transcription of a Gal4 reporter. Further analyses mapped a novel repression **domain** (RepD1) to a small region at the N-terminal portion of NRIF3 (residues 20 to 50). The NRIF3 gene encodes atomic . . . additional isoforms due to alternative splicing. These two isoforms contain the same RepD1 region as NRIF3. Consistent with this, Gal4 **fusions** of these two isoforms were also found to repress transcription. Cotransfection of NRIF3 or its two isoforms did not relieve the transrepression function mediated by their corresponding Gal4 **fusion** proteins, suggesting that the repression involves a mechanism(s) other than the recruitment of a titratable corepressor. Interestingly, a single amino. . . regulation by cellular signaling. Taken together, our results identify NRIF3 as an interesting coregulator that possesses both transactivation and transrepression **domains** and/or functions. Collectively, the NRIF3 family of coregulators (which includes NRIF3 and its other isoforms) may play dual roles in. . .

L2 ANSWER 9 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 ACCESSION NUMBER: 2001:245804 BIOSIS
 DOCUMENT NUMBER: PREV200100245804
 TITLE: Chimeric DNA-binding domain of E. coli purine repressor and yeast GAL4.

AUTHOR(S): Kim, Kyung-Sup [Reprint author]; Yeon, Eun-Hee [Reprint author]
CORPORATE SOURCE: Yonsei Univ. Col. Medicine, 134 Shinchondong Seodaemungu, Seoul, 120-752, South Korea
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A877. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002

AB Transcription activators have two modules, such as DNA-binding **domain**(DBD) and activator **domain** (ADs), which act independently. Artificial transcription factor could be created by generating chimeric **fusion** proteins between DBDs and ADs originated from different transcription activators. The development of wide spectrum of DBD enable the broader applications of artificial transcription factors. In this study, we created the new DBD by **fusion** of amino-terminal 45 residues of purine repressor DBD and **dimerization domain**(DD) of GAL4 transcription factor. The carboxy terminal 9 amino acids of 45 amino acid purine repressor and the close positioning of two purine repressor DBDs by GAL4 DD are critical to DNA-binding activity. The reconstituted DNA-binding **domain** was fused to ligand binding **domain** (LBD) of progesterone **receptor**(PR) and AD of SREBP1a, and was expressed in NIH 3T3 cells. The artificial **nuclear receptor** activated luciferase reporter expression 63 folds by addition of RU486. This activation was blunted by increasing the expression of GAL4. . . . to inactivation of DNA binding activity of purine repressor DBD-GAL4 DD by heterodimerization with GAL4 DBD. We concluded that the **fusion** of purine repressor DBD and GAL4 DD generated fully active DBD in vitro and in vivo.

L2 ANSWER 10 OF 28 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001089261 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11113190
TITLE: Oligomerization of ETO is obligatory for corepressor interaction.
AUTHOR: Zhang J; Hug B A; Huang E Y; Chen C W; Gelmetti V; Maccarana M; Minucci S; Pelicci P G; Lazar M A
CORPORATE SOURCE: Division of Endocrinology, Diabetes, and Metabolism, Departments of Medicine and Genetics, and The Penn Diabetes Center, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104, USA.
CONTRACT NUMBER: DK433806 (NIDDK)
DK45586 (NIDDK)
SOURCE: Molecular and cellular biology, (2001 Jan) 21 (1) 156-63. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB . . . a chromosomal translocation that combines a sequence-specific DNA binding protein, AML1, with a potent transcriptional repressor, ETO. ETO interacts with **nuclear receptor** corepressors SMRT and N-CoR, which recruit histone deacetylase to the AML1-ETO oncoprotein.

SMRT-N-CoR interaction requires each of two zinc fingers. . . ETO, as well as for inhibition of hematopoietic differentiation by AML1-ETO. NHR2 mediates oligomerization of ETO as well as AML1-ETO. **Fusion of NHR4 polypeptide to a heterologous dimerization domain** allows strong interaction with SMRT in vitro. These data support a model in which NHR2 and NHR4 have complementary functions in repression by ETO. NHR2 functions as an oligomerization **domain** bringing together NHR4 polypeptides that together form the surface required for high-affinity interaction with corepressors. As **nuclear receptors** also interact with corepressors as dimers, oligomerization may be a common mechanism regulating corepressor interactions.

L2 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:475956 CAPLUS
 DOCUMENT NUMBER: 133:100426
 TITLE: Fusion proteins of ligand-binding domains and dimerization domains and their uses
 INVENTOR(S): Jerome, Valerie; Sedlacek, Hans-Harald; Mueller, Rolf
 PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
 SOURCE: Ger. Offen., 36 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19900743	A1	20000713	DE 1999-19900743	19990112
CA 2359479	AA	20000720	CA 2000-2359479	20000105
WO 2000042179	A2	20000720	WO 2000-EP29	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000042179	A3	20001116	WO 2000-EP200000029	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1144634	A2	20011017	EP 2000-906186	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534121	T2	20021015	JP 2000-593736	20000105
US 6495346	B1	20021217	US 2000-481593	20000112
ZA 2001005427	A	20020716	ZA 2001-5427	20010702
US 2003054409	A1	20030320	US 2002-201949	20020725
PRIORITY APPLN. INFO.:				
			DE 1999-19900743	A 19990112
			WO 2000-EP29	W 20000105
			US 2000-481593	A1 20000112
IT Proteins, specific or class				
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)				

(ARNT (aryl hydrocarbon **receptor nuclear**
translocator), **fusion** proteins containing **dimerization**
domains of; **fusion** proteins of ligand-binding
domains and **dimerization domains** and their
uses)

L2 ANSWER 12 OF 28 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001305617 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11075811
TITLE: Regulation of ligand-induced heterodimerization and
coactivator interaction by the activation function-2 domain
of the vitamin D receptor.
AUTHOR: Liu Y Y; Nguyen C; Peleg S
CORPORATE SOURCE: Department of Medical Specialties, The University of Texas
M. D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: DK-50583 (NIDDK)
SOURCE: Molecular endocrinology (Baltimore, Md.), (2000 Nov) 14
(11) 1776-87.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531

AB . . . times more potent transcriptionally than the natural hormone. To
determine whether this enhanced activity is mediated through modulation of
the **dimerization** process or through interaction with
coactivators, we performed quantitative protein-protein interaction assays
with in vitro translated vitamin D **receptor** (ivtVDR) and
fusion proteins containing glutathione-S-transferase (GST) and
either the ligand-binding **domain** of retinoid X **receptor**
(RXRalpha), or the **nuclear receptor**-interacting
domain of the steroid **receptor** coactivator 1 (SRC-1), or
the glucocorticoid **receptor**-interacting protein 1 (GRIP-1). We
found that heterodimerization of the ligand-binding **domains** of
RXRalpha and VDR was primarily dantanoid dependent as was the interaction
of VDR with the SRC-1 or with GRIP-1. . . . interaction of VDR with
GRIP-1 (ED50 = 0.1-0.3 nM). Mutations in heptad 9 diminished both 1,25D3
and the 20-epi analog-mediated **dimerization**, without changing
binding of these ligands to VDR. Mutations in VDR's activation function 2
(AF-2) **domain**/helix 12 residues diminished the ability of 1,25D3
to induce heterodimerization and interaction with SRC-1. These mutations
did not change the ability of 20-epi-1,25D3 to induce **dimerization**
but did diminish its ability to induce interaction with SRC-1. We
hypothesize that both the hormone and the analog stabilize
receptor conformations that expose VDR's functional interfaces.
The mechanisms by which the two ligands expose these functional interfaces
differ with respect to participation of the AF-2 **domain**.

L2 ANSWER 13 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:312071 BIOSIS
DOCUMENT NUMBER: PREV200100312071
TITLE: Stat5B shuttles between cytoplasm and nucleus depending on
active nuclear import and export.
AUTHOR(S): Zeng, Rong [Reprint author]; Arai, Ken-ichi [Reprint
author]; Watanabe, Sumiko [Reprint author]
CORPORATE SOURCE: Department of Molecular and Developmental Biology,
Institute of Medical Science, University of Tokyo, Tokyo,
Japan
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp.
681a. print.

Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology. San Francisco, California, USA. December
01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 27 Jun 2001

Last Updated on STN: 19 Feb 2002

AB. . . and relocated to the cytoplasm where it can be reactivated,
completing an activation-inactivation cycle. To clarify the mechanisms
regulating the **nuclear** translocation and **nuclear**
withdrawal of Stat5, we analyzed translocation of various mutants Stat5 in
mIL-3 dependent Ba/F3 cells. We first confirmed that Stat5B, either
stably expressed as GFP **fusion** protein or transiently expressed
as FLAG **fusion** protein in Ba/F3 cells, was localized
predominantly in the cytoplasm after factor depletion, and translocated to
the nucleus upon factor stimulation. In COS7 and NIH3T3 cells,
over-expressed tagged-Stat5B mainly localized in cytoplasm. Leptomycin B
(LMB), a specific inhibitor of **nuclear** export **receptor**
CRM1, inhibited the cytoplasm accumulation of Stat5B in factor-depleted
Ba/F3 cells. The cytoplasmic localization of Stat5B in COS7 and NIH3T3.
. . . in the presence of LMB. Surprisingly, mutation of the critical
tyrosine residue Tyr699 of Stat5B did not affect this LMB-provoked
nuclear accumulation. These results suggest that tyrosine residue
independent **nuclear**/cytoplasm shuttling exist regardless of
cytokine stimulation and **nuclear** export of STAT5B is CRM1
dependent. Furthermore, we identified an amino-terminal leucine
zipper-like region and a region surrounding **dimerization**
domain of Stat5B critical for its active **nuclear** import
and export, respectively. Our results suggest that Stats shuttle between
the cytoplasm and the nucleus in both factor dependent and independent
manners, and subcellular distribution of Stat5 depends on the balance
between the constitutive Stat5 **nuclear** import and the
dimerization-regulated Stat5 **nuclear** export.

L2 ANSWER 14 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:300212 BIOSIS

DOCUMENT NUMBER: PREV200100300212

TITLE: Pediatric ALK-positive lymphomas coexpress C-Myc.

AUTHOR(S): Raetz, Elizabeth A. [Reprint author]; Perkins, Sherrie L.;
Carlson, Marlee A. [Reprint author]; Schooler, Kevin P.;
Virshup, David M. [Reprint author]

CORPORATE SOURCE: Pediatrics, University of Utah/Huntsman Cancer Institute,
Salt Lake City, UT, USA

SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp.
128a. print.

Meeting Info.: 42nd Annual Meeting of the American Society
of Hematology. San Francisco, California, USA. December
01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 20 Jun 2001

Last Updated on STN: 19 Feb 2002

AB The majority of pediatric anaplastic large cell lymphomas (ALCL) carry a
specific chromosomal translocation, t(2;5)(p23;q35) that juxtaposes the
putative **dimerization domain** of nucleophosmin (NPM)
with the orphan **receptor** tyrosine kinase, anaplastic lymphoma
kinase (ALK). The NPM-ALK **fusion** appears to induce
constitutive, ligand-independent activation of the ALK protein leading to

aberrant phosphorylation of other cellular signaling proteins. To further study the early consequences of aberrant ALK activation, we constructed a Myc epitope tagged GyrB-ALK **fusion** that allows regulated **dimerization**. We utilized coumermycin to induce **dimerization** and subsequent activation of the GyrB-ALK **fusion**. A dose-dependent increase in tyrosine phosphorylation of the GyrB-ALK **fusion** was seen following the addition of drug to both reticulocyte lysates and fibroblast cell lines expressing the **fusion** construct. We also observed a dose-dependent increase in the level of tyrosine phosphorylation of other undefined cellular proteins after coumermycin treatment, suggesting that ALK activation by **dimerization** leads not only to autophosphorylation, but also to the direct, or indirect modification of other cellular proteins. While performing gene dosage studies with the GyrB-ALK **fusion** construct, we observed an increase in the expression of a protein the approximate size of c-Myc by Western blotting. We extended. . . significance of this finding, we investigated expression patterns of c-Myc and ALK by immunohistochemical analysis in childhood ALCL tumor samples. **Nuclear** co-expression of c-Myc and ALK was seen in tumor cells in 15 of 15 (100%) ALCL samples carrying the t(2;5). . .

L2 ANSWER 15 OF 28 MEDLINE on STN DUPLICATE 7
 ACCESSION NUMBER: 1999395139 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10464303
 TITLE: Evidence for a novel cardiac-enriched retinoid X receptor partner.
 AUTHOR: Cresci S; Clabby M L; Kelly D P
 CORPORATE SOURCE: Center for Cardiovascular Research, Washington University School of Medicine, St. Louis, Missouri 62110, USA.
 CONTRACT NUMBER: F32-HL09189 (NHLBI)
 RO1-HL58493 (NHLBI)
 SOURCE: Journal of biological chemistry, (1999 Sep 3) 274 (36) 25668-74.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199910
 ENTRY DATE: Entered STN: 19991014
 Last Updated on STN: 19991014
 Entered Medline: 19991007

AB . . . a pivotal role in cardiac morphogenesis and function. To identify proteins that serve as interacting partners of the retinoid X **receptor** alpha (RXRalpha) in heart, DNA-protein binding studies were performed with an RXR-responsive element (NRRE-1) derived from the medium chain acyl-CoA dehydrogenase gene promoter and **nuclear** protein extracts prepared from adult rat heart. NRRE-1 is a pleiotropic RXR-responsive element comprised of three potential recognition sites for class II members of the **nuclear receptor** superfamily. Gel mobility shift assays performed with an NRRE-1 probe in the absence or presence of bacterially overproduced RXRalpha and **nuclear** protein extracts prepared from adult rat heart, liver, or brain identified a cardiac-specific, RXR-dependent DNA-protein interaction. The NRRE-1-RXR cardiac-enriched RXR-interacting protein (CERIP) complex exhibited a distinct mobility compared with NRRE-1-RXR.peroxisome proliferator-activated **receptor**, NRRE-1-RXR.retinoic acid **receptor**, or NRRE-1-RXR.thyroid **receptor** complexes. Mutational analysis demonstrated that two of the three potential binding half-sites of NRRE-1 (an everted repeat separated by an. . . CERIP interaction. Gel mobility shift assays demonstrated that CERIP interacted with RXRalpha and RXRgamma but not with RXRbeta, indicating a **receptor** subtypespecific binding preference and suggesting an RXR AB region-dependent interaction. The RXR.CERIP complex did not form on

NRRE-1 when a mutant GST-RXRalpha **fusion** protein lacking the NH(2)-terminal AB region (but containing the **receptor dimerization domain**) of RXRalpha was added in place of the full-length RXRalpha, confirming a role for the AB region in the RXR..

L2 ANSWER 16 OF 28 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000065098 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10597230
TITLE: Formation of PML/RAR alpha high molecular weight nuclear complexes through the PML coiled-coil region is essential for the PML/RAR alpha-mediated retinoic acid response.
AUTHOR: Grignani F; Gelmetti V; Fanelli M; Rogaia D; De Matteis S; Ferrara F F; Bonci D; Grignani F; Nervi C; Pelicci P G
CORPORATE SOURCE: Istituto di Medicina Interna e Scienze Oncologiche, Policlinico Montelucente, Perugia, Italy.
SOURCE: Oncogene, (1999 Nov 4) 18 (46) 6313-21.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000110

AB . . . RA-sensitivity in APL is mediated by its oncogenic protein, which results from the recombination of the PML and the RA **receptor** alpha (RAR alpha) genes (PML/RAR alpha **fusion** protein). Ectopic expression of PML/RAR alpha into haemopoietic cell lines results in increased response to RA-induced differentiation. By structure-function analysis of PML/RAR alpha-mediated RA-differentiation, we demonstrated that **fusion** of PML and RAR alpha sequences and integrity of the PML **dimerization domain** and of the RAR alpha DNA binding region are required for the effect of PML/RAR alpha on RA-differentiation. Indeed, direct **fusion** of the PML **dimerization domain** to the N- or C-terminal extremities of RAR alpha retained full biological activity. All the biologically active PML/RAR alpha mutants formed high molecular weight complexes in vivo. Functional analysis of mutations within the PML **dimerization domain** revealed that the capacity to form PML/RAR alpha homodimers, but not PML/RAR alpha-PML heterodimers, correlated with the RA-response. These results suggest that targeting of RAR alpha sequences by the PML **dimerization domain** and formation of **nuclear** PML/RAR alpha homodimeric complexes are crucial for the ability of PML/RAR alpha to mediate RA-response.

L2 ANSWER 17 OF 28 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1998241632 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9575217
TITLE: Jak2-Stat5 interactions analyzed in yeast.
AUTHOR: Barahmand-Pour F; Meinke A; Groner B; Decker T
CORPORATE SOURCE: Institute of Microbiology and Genetics, Vienna Biocenter, University of Vienna, Dr. Bohr-Gasse 9, A-1030 Vienna, Austria.
SOURCE: Journal of biological chemistry, (1998 May 15) 273 (20) 12567-75.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980625

Last Updated on STN: 19980625

Entered Medline: 19980612

AB Many cytokine **receptors** employ Janus protein tyrosine kinases (Jaks) and signal transducers and activators of transcription (Stats) for **nuclear** signaling. Here, we have established yeast strains in which an autoactivated Jak2 kinase induces tyrosine phosphorylation, **dimerization**, **nuclear** translocation, and DNA binding of a concomitantly expressed Stat5 protein. Transcriptional activity of Stat5 on a stably integrated, Stat-dependent reporter gene required the C-terminal **fusion** of the VP16 transactivation **domain**. In such yeast strains, the interaction between Jak2 and Stat5 was analyzed without interference by other mammalian proteins involved in. . . be stable under stringent co-immunoprecipitation conditions. Deletion of the Jak homology regions 2-7 (JH2-JH7) of Jak2, leaving only the kinase **domain** (JH1) intact, reduced the ability of the kinase to phosphorylate Stat5, whereas deletion of the JH2 **domain** caused an increased enzymatic activity. A site-directed R618K mutation in the Stat5 SH2 **domain** abolished the phosphorylation by Jak2, while deletion of the C terminus led to Stat5 hyperphosphorylation. A single phosphotyrosine-SH2 **domain** interaction was sufficient for the **dimerization** of Stat5, but such dimers bound to DNA very inefficiently. Together, our data show that yeast cells are appropriate tools for studying Jak-Stat or Stat-Stat interactions. Our mutational analysis suggests that the Stat5 SH2 **domain** is essential for the interaction with Jak2 and that the kinase **domain** of Jak2 is sufficient for Jak2-Stat5 interaction. Therefore, the Jak kinase **domain** may be all that is needed to cause Stat phosphorylation in situations where **receptor** docking is dispensable.

L2 ANSWER 18 OF 28 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 97294712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9148917
TITLE: Thyroid hormone-mediated enhancement of heterodimer formation between thyroid hormone receptor beta and retinoid X receptor.
AUTHOR: Collingwood T N; Butler A; Tone Y; Clifton-Bligh R J; Parker M G; Chatterjee V K
CORPORATE SOURCE: Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom.
SOURCE: Journal of biological chemistry, (1997 May 16) 272 (20) 13060-5.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970619

AB A subset of **nuclear receptors**, including those for thyroid hormone (TR), retinoic acid, vitamin D3, and eicosanoids, can form heterodimers with the retinoid X **receptor** (RXR) on DNA regulatory elements in the absence of their cognate ligands. In a mammalian two-hybrid assay, we have found that recruitment of a VP16-RXR chimera by a Gal4-TRbeta ligand-binding **domain fusion** is enhanced up to 50-fold by thyroid hormone (T3). This was also observed with a mutant **fusion**, Gal4-TR(L454A), lacking ligand-inducible activation function (AF-2) and unable to interact with putative coactivators, suggesting that the AF-2 activity of TR or intermediary cofactors is not involved in this effect. The wild-type and mutant Gal4-TR **fusions** also exhibited hormone-dependent recruitment of RXR in yeast. Hormone-dependent recruitment of RXR was also evident with another Gal4-TR mutant, AHTm, which does not interact with the

nuclear receptor corepressor N-CoR, suggesting that ligand-enhanced **dimerization** is not a result of T3-induced corepressor release. Finally, we have shown that the interaction between RXR and TR is. . . effect. We propose that ligand-dependent heterodimerization of TR and RXR in solution may provide a further level of control in **nuclear receptor** signaling.

L2 ANSWER 19 OF 28 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 97297774 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9153406
TITLE: The isolation and characterization of purified heterocomplexes of recombinant retinoic acid receptor and retinoid X receptor ligand binding domains.
AUTHOR: Tian K; Norris A W; Lin C L; Li E
CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: 5-T32GM07200 (NIGMS)
DK40172 (NIDDK)
DK49684 (NIDDK)
SOURCE: Biochemistry, (1997 May 13) 36 (19) 5669-76.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970609
AB Retinoic acid exerts many of its biological effects by interaction with heterocomplexes of **nuclear** retinoic acid **receptors** (RARs) and retinoid X **receptors** (RXRs). To further examine this interaction, a glutathione S-transferase (GST) **fusion** protein containing the ligand binding **domain** of human RXR alpha has been used to copurify the ligand binding **domain** of human RAR gamma by affinity chromatography over glutathione-agarose. Complexes of recombinant RAR-RXR ligand binding **domains** retaining full ligand binding capacity were purified, and their interactions with various retinoids were characterized by fluorometric titration and photoaffinity. . . These results suggest that certain retinoids could potentially perturb the distribution of endogenous retinoic acid between the CRABPs and the **nuclear receptors** and thus affect retinoid signaling. The purified recombinant complexes should provide a useful model system for further structural analysis of the **dimerization** interface between the RAR and RXR ligand binding **domains**.

L2 ANSWER 20 OF 28 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 97220023 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9121481
TITLE: Role of the nucleophosmin (NPM) portion of the non-Hodgkin's lymphoma-associated NPM-anaplastic lymphoma kinase fusion protein in oncogenesis.
AUTHOR: Bischof D; Pulford K; Mason D Y; Morris S W
CORPORATE SOURCE: Department of Experimental Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee 38105, USA.
CONTRACT NUMBER: CA 01702 (NCI)
CA 27165 (NCI)
CA 69129 (NCI)
SOURCE: Molecular and cellular biology, (1997 Apr) 17 (4) 2312-25.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19980206
Entered Medline: 19970424

AB The NPM-ALK **fusion** gene, formed by the t(2;5)(p23;q35) translocation in non-Hodgkin's lymphoma, encodes a 75-kDa hybrid protein that contains the amino-terminal 117 amino acid residues of the nucleolar phosphoprotein nucleophosmin (NPM) joined to the entire cytoplasmic portion of the **receptor** tyrosine kinase ALK (anaplastic lymphoma kinase). Here, we demonstrate the transforming ability of NPM-ALK and show that oncogenesis by the . . . fractionation studies of the t(2;5) translocation-containing lymphoma cell line SUP-M2 showed NPM-ALK to be localized within both the cytoplasmic and **nuclear** compartments. Immunostaining performed with both polyclonal and monoclonal anti-ALK antibodies confirmed the dual location of the oncoprotein and also indicated. . . form complexes, lacked kinase activity in vivo, and failed to transform cells. However, NPM could be functionally replaced in the **fusion** protein with the portion of the unrelated translocated promoter region (TPR) protein that activates the TPR-MET **fusion** kinase by mediating **dimerization** through its leucine zipper motif. This engineered TPR-ALK hybrid protein, which transformed cells almost as efficiently as NPM-ALK, was localized solely within the cytoplasm of cells. These data indicate that the **nuclear** and nucleolar localization of NPM-ALK, which probably occur because of transport via the shuttling activity of NPM, is not required for oncogenesis. Further, the activation of the truncated ALK protein by a completely heterologous oligomerization **domain** suggests that the functionally important role of the NPM segment of NPM-ALK in transformation is restricted to the formation of. . .

L2 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:511309 BIOSIS
DOCUMENT NUMBER: PREV199699233665
TITLE: Effects of differentiation by the promyelocytic leukemia PML/RAR-alpha protein depend on the fusion of the PML protein dimerization and RAR-alpha DNA binding domains.
AUTHOR(S): Grignani, Francesco; Testa, Ugo; Rogaia, Daniela; Ferrucci, Pier Francesco; Samoggia, Paola; Pinto, Antonello; Aldinucci, Donatella; Gelmetti, Vania; Fagioli, Marta; Alcalay, Myriam; Seeler, Jacob; Grignani, Fausto; Nicoletti, Ildo; Peschle, Cesare; Pelicci, Pier Giuseppe [Reprint author]
CORPORATE SOURCE: Ist. Clin. Med. I, Policlin. Monteluce, Perugia Univ., 06100 Perugia, Italy
SOURCE: EMBO (European Molecular Biology Organization) Journal, (1996) Vol. 15, No. 18, pp. 4949-4958.
CODEN: EMJODG. ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 1996
Last Updated on STN: 14 Nov 1996

IT Miscellaneous Descriptors
ACUTE PROMYELOCYTIC LEUKEMIA; BLOOD AND LYMPHATIC DISEASE;
DIMERIZATION; DNA BINDING **DOMAINS**; **FUSION**
PROTEIN; NEOPLASTIC DISEASE; **NUCLEAR** PROTEIN; ONCOGENIC
ACTIVITY; PML PROTEIN; PML/RAR-ALPHA PROTEIN; PML/RETINOIC ACID
RECEPTOR-ALPHA PROTEIN; RAR-ALPHA; RETINOIC ACID
RECEPTOR-ALPHA; TRANSCRIPTION FACTOR; TUMOR BIOLOGY

L2 ANSWER 22 OF 28 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 96189072 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8628257
TITLE: Transcriptional silencing by unliganded thyroid hormone receptor beta requires a soluble corepressor that interacts

with the ligand-binding domain of the receptor.

AUTHOR: Tong G X; Jeyakumar M; Tanen M R; Bagchi M K
 CORPORATE SOURCE: Population Council and the Rockefeller University, New York, NY 10021, USA.
 CONTRACT NUMBER: R01 DK 50257-01 (NIDDK)
 SOURCE: Molecular and cellular biology, (1996 May) 16 (5) 1909-20.
 Journal code: 8109087. ISSN: 0270-7306.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199606
 ENTRY DATE: Entered STN: 19960708
 Last Updated on STN: 19980206
 Entered Medline: 19960621

AB Unliganded thyroid hormone **receptor** (TR) functions as a transcriptional repressor of genes bearing thyroid hormone response elements in their promoters. Binding of hormonal ligand to the **receptor** releases the transcriptional silencing and leads to gene activation. Previous studies showed that the silencing activity of TR is located within the C-terminal ligand-binding **domain** (LBD) of the **receptor**. To dissect the role of the LBD in **receptor**-mediated silencing, we used a cell-free transcription system containing HeLa **nuclear** extracts in which exogenously added unliganded TRbeta repressed the basal level of RNA polymerase II-driven transcription from a thyroid hormone. . . with a peptide fragment containing the entire LBD (positions 145 to 456) of TRbeta. This peptide, which lacks the DNA-binding **domain**, did not affect basal RNA synthesis from the thyroid hormone response element-linked promoter when added to a cell-free transcription reaction. . . mixture. However, the addition of the LBD peptide to a reaction mixture containing TRbeta led to a complete reversal of **receptor**-mediated transcriptional silencing in the absence of thyroid hormone. An LBD peptide harboring point mutations, which severely impair **receptor dimerization**, also inhibited efficiently the silencing activity of TR, indicating that the relief of repression by the LBD was not due to the sequestration of TR or its heterodimeric partner retinoid X **receptor** into inactive homo- or heterodimers. We postulate that the LBD peptide competed with TR for a regulatory molecule, termed a corepressor, that exists in the HeLa **nuclear** extracts and is essential for efficient **receptor**-mediated gene repression. We have identified the region from positions 145 to 260 (the D **domain**) of the LBD as a potential binding site of the putative corepressor. We observed further that a peptide containing the LBD of retinoic acid **receptor** (RAR) competed for TR-mediated silencing, suggesting that the RAR LBD may bind to the same corepressor activity as the TR. . . corepressor is ligand dependent. Finally, we provide strong biochemical evidence supporting the existence of the corepressor activity in the HeLa **nuclear** extracts. Our studies demonstrated that the silencing activity of TR was greatly reduced in the **nuclear** extracts preincubated with immobilized, hormone-free glutathione S-transferase-LBD **fusion** proteins, indicating that the corepressor activity was depleted from these extracts through protein-protein interactions with the LBD. Similar treatment with immobilized, hormone-bound glutathione S-transferase-LBD, on the other hand, failed to deplete the corepressor activity from the **nuclear** extracts, indicating that ligand binding to the LBD disrupts its interaction with the corepressor. From these results, we propose that a corepressor binds to the LBD of unliganded TR and critically influences the interaction of the **receptor** with the basal transcription machinery to promote silencing. Ligand binding to TR results in the release of the corepressor from. . .

DOCUMENT NUMBER: PubMed ID: 8643677
TITLE: In vivo and in vitro characterization of the B1 and B2 zinc-binding domains from the acute promyelocytic leukemia protooncoprotein PML.
AUTHOR: Borden K L; Lally J M; Martin S R; O'Reilly N J; Solomon E; Freemont P S
CORPORATE SOURCE: Protein Structure Laboratory, Imperial Cancer Research Fund, London, United Kingdom.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996 Feb 20) 93 (4) 1601-6. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 19970203
Entered Medline: 19960717

AB Acute promyelocytic leukemia (APL) has been ascribed to a chromosomal translocation event which results in a **fusion** protein comprising the PML protein and retinoic acid **receptor** alpha. PML is normally a component of a **nuclear** multiprotein complex which is disrupted in the APL disease state. Here, two newly defined cysteine/histidine-rich protein motifs called the B-box (B1 and B2) from PML have been characterized in terms of their effect on PML **nuclear** body formation, their **dimerization**, and their biophysical properties. We have shown that both peptides bind Zn²⁺, which induces changes in the peptides' structures. We demonstrate that mutants in both B1 and B2 do not form PML **nuclear** bodies in vivo and have a phenotype that is different from that observed in the APL disease state. Interestingly, these . . . not affect the ability of wild-type PML to dimerize with mutant proteins in vitro, suggesting that the B1 and B2 **domains** are involved in an additional interaction central to PML **nuclear** body formation. This report in conjunction with our previous work demonstrates that the PML RING-B1/B2 motif plays a fundamental role. . .

L2 ANSWER 24 OF 28 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 96239489 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8657108
TITLE: The t(12;21) translocation converts AML-1B from an activator to a repressor of transcription.
AUTHOR: Hiebert S W; Sun W; Davis J N; Golub T; Shurtleff S; Buijs A; Downing J R; Grosveld G; Russell M F; Gilliland D G; Lenny N; Meyers S
CORPORATE SOURCE: Department of Tumor Cell Biology, St. Jude Children's Research Hospital, Memphis, Tennessee 38105, USA.
CONTRACT NUMBER: CA-57261 (NCI)
RO1 CA-56819 (NCI)
RO1 CA-64140 (NCI)
SOURCE: Molecular and cellular biology, (1996 Apr) 16 (4) 1349-55. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960729

AB The t(12;21) translocation is present in up to 30% of childhood B-cell acute lymphoblastic and fuses a potential **dimerization** motif from the ets-related factor TEL to the N terminus of AML1. The t(12;21)

translocation encodes a 93-kDa **fusion** protein that localizes to a high-salt- and detergent-resistant **nuclear** compartment. This protein binds the enhancer core motif, TGTGGT, and interacts with the AML-1-binding protein, core-binding factor beta. Although TEL/AML-1B retains the C-terminal **domain** of AML-1B that is required for transactivation of the T-cell **receptor** beta enhancer, it fails to activate transcription but rather inhibits the basal activity of this enhancer. TEL/AML-1B efficiently interferes with AML-1B dependent transactivation of the T-cell **receptor** beta enhancer, and coexpression of wild-type TEL does not reverse this inhibition. The N-terminal TEL helix-loop-helix **domain** is essential for TEL/AML-1B-mediated repression. Thus, the t(12;21) **fusion** protein dominantly interferes with AML-1B-dependent transcription, suggesting that the inhibition of expression of AML-1 genes is critical for B-cell leukemogenesis.

L2 ANSWER 25 OF 28 MEDLINE on STN DUPLICATE 16
 ACCESSION NUMBER: 95081092 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7989319
 TITLE: Potent transactivation domains of the Ah receptor and the Ah receptor nuclear translocator map to their carboxyl termini.
 AUTHOR: Jain S; Dolwick K M; Schmidt J V; Bradfield C A
 CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, Illinois 60611.
 CONTRACT NUMBER: ES05703 (NIEHS)
 T32 CA09560 (NCI)
 T32 ES07124 (NIEHS)
 SOURCE: Journal of biological chemistry, (1994 Dec 16) 269 (50) 31518-24.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199501
 ENTRY DATE: Entered STN: 19950124
 Last Updated on STN: 19950124
 Entered Medline: 19950112

AB The Ah **receptor** (AHR) is a ligand-activated transcription factor that is structurally related to its **dimerization** partner, the Ah **receptor nuclear** translocator (ARNT), and two Drosophila proteins, SIM and PER. All four proteins contain a region of homology now referred to as a PAS homology **domain**. In addition, the AHR, ARNT, and SIM harbor a basic region helix-loop-helix motif in their N termini, whereas PER does not. Previous mapping studies of the AHR have demonstrated that the PAS **domain** contains sequences required for ligand recognition, **dimerization**, and interaction with the 90-kDa heat shock protein. They also have confirmed that the basic region helix-loop-helix **domain** plays a role in both **dimerization** and sequence-specific DNA binding. To identify **domains** involved in transactivation of target genes, we generated chimeras of AHR/ARNT deletion mutants with the DNA binding region of the . . . reporter gene under the control of a minimal promoter driven by enhancer elements recognized by Gal4. Extensive analysis of these **fusions** revealed that the AHR and ARNT harbor potent transactivation **domains** within their C termini. Importantly, the amino-terminal halves of both the AHR and ARNT were found to be devoid of. . .

L2 ANSWER 26 OF 28 MEDLINE on STN DUPLICATE 17
 ACCESSION NUMBER: 94022372 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8415704

TITLE: The PML-retinoic acid receptor alpha translocation converts the receptor from an inhibitor to a retinoic acid-dependent activator of transcription factor AP-1.

AUTHOR: Doucas V; Brockes J P; Yaniv M; de The H; Dejean A

CORPORATE SOURCE: Departement des Biotechnologies, Institut Pasteur, Paris, France.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 15) 90 (20) 9345-9. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931119

AB We report here that the **fusion** of PML, a **nuclear** protein defined by the t(15;17) chromosomal translocation in acute promyelocytic leukemia, with retinoic acid **receptor** alpha (RAR alpha) changes the RAR alpha from a retinoic acid (RA)-dependent inhibitor to a RA-dependent activator of AP-1 transcriptional. . . a circumstance in which RAR alpha has no effect on AP-1 activity, PML-RAR alpha is an inhibitor. Deletion of the **dimerization**, transactivation, or DNA-binding **domains** of c-Jun and removal of the PML **dimerization domain** in the PML-RAR alpha hybrid abrogates their transcriptional cooperatively. In view of the association between AP-1 activity and hemopoietic differentiation, . . .

L2 ANSWER 27 OF 28 MEDLINE on STN DUPLICATE 18

ACCESSION NUMBER: 94038899 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8223432

TITLE: Definition of a novel ligand binding domain of a nuclear bHLH receptor: co-localization of ligand and hsp90 binding activities within the regulable inactivation domain of the dioxin receptor.

AUTHOR: Whitelaw M L; Gottlicher M; Gustafsson J A; Poellinger L

CORPORATE SOURCE: Department of Medical Nutrition, Karolinska Institutet, Huddinge University Hospital, Sweden.

SOURCE: EMBO journal, (1993 Nov) 12 (11) 4169-79. Journal code: 8208664. ISSN: 0261-4189.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199312

ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931206

AB The dioxin **receptor** mediates signal transduction by dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin) and binds to DNA target sequences as a heterodimer of the approximately 100 kDa ligand binding **receptor** and the approximately 85 kDa auxiliary factor, Arnt. Both of these factors encompass an N-terminal basic helix-loop-helix (bHLH) motif required for DNA binding and **dimerization**. In this study we describe the construction of glucocorticoid/dioxin **receptor fusion** proteins which allow the regulation of glucocorticoid **receptor** activity by dioxin in transient transfections of CHO and hepatoma cells. Thus, in the absence of dioxin, chimeric **receptor** constructs which contain large 500-720 amino acid C-terminal dioxin **receptor** fragments, but lack the N-terminal bHLH motif, confer repression upon the transcriptional activity of a glucocorticoid **receptor** derivative, tau DBD, containing its N-terminal strong transactivating signal (tau) and its DNA binding **domain** (DBD).

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.E5
p27

In the presence of dioxin, this repression is reversed. Importantly, these chimeric **receptors** did not require the bHLH Arnt co-factor for function. A considerably smaller region of the dioxin **receptor**, located between amino acids 230 and 421, showed specific dioxin binding activity in vitro. Moreover, dioxin binding in vitro correlated with the ability of **receptor** fragments to form stable complexes in vitro with the molecular chaperone hsp90. These findings support the notion that hsp90 may be important for folding of a dioxin binding configuration of the **receptor**. Finally, tau DBD activity was constitutively repressed in a dioxin non-responsive manner by dioxin **receptor** fragments which failed to bind ligand but also failed to bind hsp90 in vitro, indicating that alternative mechanisms in addition to hsp90 binding may contribute to the inactivation function. In summary, the dioxin **receptor** system provides a novel and complex model of regulation of bHLH factors that may also give important insights into the mechanism of action of ligand-activated **nuclear receptors**.

L2 ANSWER 28 OF 28 MEDLINE on STN DUPLICATE 19
 ACCESSION NUMBER: 93327770 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8334997
 TITLE: Hormone-conditional transformation by fusion proteins of c-Abl and its transforming variants.
 AUTHOR: Jackson P; Baltimore D; Picard D
 CORPORATE SOURCE: Departement de Biologie Cellulaire, Universite de Geneve, Sciences III, Switzerland.
 CONTRACT NUMBER: CA51462 (NCI)
 SOURCE: EMBO journal, (1993 Jul) 12 (7) 2809-19.
 Journal code: 8208664. ISSN: 0261-4189.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199308
 ENTRY DATE: Entered STN: 19930903
 Last Updated on STN: 19970203
 Entered Medline: 19930820

AB **Fusion** of the hormone binding **domain** (HBD) of steroid **receptors** to transcription factors renders them hormone-dependent. We show here that an SH3-deleted, oncogenic variant of the Abl tyrosine kinase becomes hormone-dependent for transformation by **fusion** to the estrogen **receptor** (ER) HBD, extending the phenomenon to tyrosine kinases. Surprisingly, **fusion** of the HBD to the normal, non-transforming c-Abl (IV) protein activated transforming activity in a hormone-dependent fashion. In the presence of hormone, the c-Abl:ER **fusion** protein was transforming, cytoplasmic and tyrosine phosphorylated, whereas it was non-transforming, **nuclear** and hypophosphorylated without hormone. We have examined the kinetics of activation of the c-Abl:ER protein and found that protein synthesis. . . c-Abl:ER protein from the nucleus to the cytoplasm. We suggest that the activation of c-Abl could be due to HBD-mediated **dimerization** and/or to the ability to overexpress conditionally the normally toxic c-Abl protein. This novel approach may be applicable to a. . .

=> d his

(FILE 'HOME' ENTERED AT 13:22:44 ON 04 AUG 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 13:22:53 ON 04 AUG 2004

L1 84 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION
 L2 28 DUP REM L1 (56 DUPLICATES REMOVED)
 L3 12 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION (
 L4 3 DUP REM L3 (9 DUPLICATES REMOVED)

L5 40 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) CHIMERA
L6 10 DUP REM L5 (30 DUPLICATES REMOVED)

=> s l4 l5 l6

MISSING OPERATOR L4 L5

The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l4 and l5 and l6

L7 3 L4 AND L5 AND L6

=> dup rem l7

PROCESSING COMPLETED FOR L7

L8 3 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 total ibib kwic

L8 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 97294712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9148917
TITLE: Thyroid hormone-mediated enhancement of heterodimer
formation between thyroid hormone receptor beta and
retinoid X receptor.
AUTHOR: Collingwood T N; Butler A; Tone Y; Clifton-Bligh R J;
Parker M G; Chatterjee V K
CORPORATE SOURCE: Department of Medicine, University of Cambridge,
Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom.
SOURCE: Journal of biological chemistry, (1997 May 16) 272 (20)
13060-5.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970619
AB A subset of **nuclear receptors**, including those for
thyroid hormone (TR), retinoic acid, vitamin D3, and eicosanoids, can form
heterodimers with the retinoid X **receptor** (RXR) on DNA
regulatory elements in the absence of their cognate ligands. In a
mammalian two-hybrid assay, we have found that recruitment of a VP16-RXR
chimera by a Gal4-TRbeta ligand-binding **domain**
fusion is enhanced up to 50-fold by thyroid hormone (T3). This
was also observed with a mutant **fusion**, Gal4-TR(L454A), lacking
ligand-inducible activation function (AF-2) and unable to interact with
putative coactivators, suggesting that the AF-2 activity of TR or
intermediary cofactors is not involved in this effect. The wild-type and
mutant Gal4-TR **fusions** also exhibited hormone-dependent
recruitment of RXR in yeast. Hormone-dependent recruitment of RXR was
also evident with another Gal4-TR mutant, AHTm, which does not interact
with the **nuclear receptor** corepressor N-CoR,
suggesting that ligand-enhanced **dimerization** is not a result of
T3-induced corepressor release. Finally, we have shown that the
interaction between RXR and TR is. . . effect. We propose that
ligand-dependent heterodimerization of TR and RXR in solution may provide
a further level of control in **nuclear receptor**
signaling.

L8 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 95081092 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7989319
TITLE: Potent transactivation domains of the Ah receptor and the

Ah receptor nuclear translocator map to their carboxyl termini.

AUTHOR: Jain S; Dolwick K M; Schmidt J V; Bradfield C A
CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, Illinois 60611.
CONTRACT NUMBER: ES05703 (NIEHS)
T32 CA09560 (NCI)
T32 ES07124 (NIEHS)
SOURCE: Journal of biological chemistry, (1994 Dec 16) 269 (50) 31518-24.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950124
Last Updated on STN: 19950124
Entered Medline: 19950112

AB The Ah **receptor** (AHR) is a ligand-activated transcription factor that is structurally related to its **dimerization** partner, the Ah **receptor nuclear translocator** (ARNT), and two Drosophila proteins, SIM and PER. All four proteins contain a region of homology now referred to as a PAS homology **domain**. In addition, the AHR, ARNT, and SIM harbor a basic region helix-loop-helix motif in their N termini, whereas PER does not. Previous mapping studies of the AHR have demonstrated that the PAS **domain** contains sequences required for ligand recognition, **dimerization**, and interaction with the 90-kDa heat shock protein. They also have confirmed that the basic region helix-loop-helix **domain** plays a role in both **dimerization** and sequence-specific DNA binding. To identify **domains** involved in transactivation of target genes, we generated **chimeras** of AHR/ARNT deletion mutants with the DNA binding region of the yeast Gal4 protein, transiently expressed these in COS-1 cells, . . . reporter gene under the control of a minimal promoter driven by enhancer elements recognized by Gal4. Extensive analysis of these **fusions** revealed that the AHR and ARNT harbor potent transactivation **domains** within their C termini. Importantly, the amino-terminal halves of both the AHR and ARNT were found to be devoid of. . .

L8 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 94022372 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8415704
TITLE: The PML-retinoic acid receptor alpha translocation converts the receptor from an inhibitor to a retinoic acid-dependent activator of transcription factor AP-1.
AUTHOR: Doucas V; Brookes J P; Yaniv M; de The H; Dejean A
CORPORATE SOURCE: Departement des Biotechnologies, Institut Pasteur, Paris, France.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 15) 90 (20) 9345-9.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931119

AB We report here that the **fusion** of PML, a **nuclear** protein defined by the t(15;17) chromosomal translocation in acute

promyelocytic leukemia, with retinoic acid **receptor** alpha (RAR alpha) changes the RAR alpha from a retinoic acid (RA)-dependent inhibitor to a RA-dependent activator of AP-1 transcriptional activity. The PML-RAR alpha **chimera** cooperates with c-Jun and, strikingly, with c-Fos to stimulate the transcription of both synthetic and natural reporter genes containing an. . . a circumstance in which RAR alpha has no effect on AP-1 activity, PML-RAR alpha is an inhibitor. Deletion of the **dimerization**, transactivation, or DNA-binding **domains** of c-Jun and removal of the PML **dimerization domain** in the PML-RAR alpha hybrid abrogates their transcriptional cooperatively. In view of the association between AP-1 activity and hemopoietic differentiation,. . .

=> d his

(FILE 'HOME' ENTERED AT 13:22:44 ON 04 AUG 2004)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 13:22:53 ON 04 AUG 2004

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L1      84 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION
L2      28 DUP REM L1 (56 DUPLICATES REMOVED)
L3      12 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) FUSION (
L4      3 DUP REM L3 (9 DUPLICATES REMOVED)
L5      40 S DIMERIZATION (P) DOMAIN (P) NUCLEAR (P) RECEPTOR (P) CHIMERA
L6      10 DUP REM L5 (30 DUPLICATES REMOVED)
L7      3 S L4 AND L5 AND L6
L8      3 DUP REM L7 (0 DUPLICATES REMOVED)
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=> d l4 total ibib kwic

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L4  ANSWER 1 OF 3      MEDLINE on STN      DUPLICATE 1
ACCESSION NUMBER:    97294712      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 9148917
TITLE:               Thyroid hormone-mediated enhancement of heterodimer
                     formation between thyroid hormone receptor beta and
                     retinoid X receptor.
AUTHOR:              Collingwood T N; Butler A; Tone Y; Clifton-Bligh R J;
                     Parker M G; Chatterjee V K
CORPORATE SOURCE:    Department of Medicine, University of Cambridge,
                     Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom.
SOURCE:              Journal of biological chemistry, (1997 May 16) 272 (20)
                     13060-5.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:        Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:             English
FILE SEGMENT:         Priority Journals
ENTRY MONTH:          199706
ENTRY DATE:           Entered STN: 19970630
                     Last Updated on STN: 19970630
                     Entered Medline: 19970619

AB  A subset of nuclear receptors, including those for
    thyroid hormone (TR), retinoic acid, vitamin D3, and eicosanoids, can form
    heterodimers with the retinoid X receptor (RXR) on DNA
    regulatory elements in the absence of their cognate ligands. In a
    mammalian two-hybrid assay, we have found that recruitment of a VP16-RXR
chimera by a Gal4-TRbeta ligand-binding domain
fusion is enhanced up to 50-fold by thyroid hormone (T3). This
    was also observed with a mutant fusion, Gal4-TR(L454A), lacking
    ligand-inducible activation function (AF-2) and unable to interact with
    putative coactivators, suggesting that the AF-2 activity of TR or
    intermediary cofactors is not involved in this effect. The wild-type and
    mutant Gal4-TR fusions also exhibited hormone-dependent
    recruitment of RXR in yeast. Hormone-dependent recruitment of RXR was
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also evident with another Gal4-TR mutant, AHTm, which does not interact with the **nuclear receptor** corepressor N-CoR, suggesting that ligand-enhanced **dimerization** is not a result of T3-induced corepressor release. Finally, we have shown that the interaction between RXR and TR is. . . effect. We propose that ligand-dependent heterodimerization of TR and RXR in solution may provide a further level of control in **nuclear receptor** signaling.

L4 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 95081092 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7989319
 TITLE: Potent transactivation domains of the Ah receptor and the Ah receptor nuclear translocator map to their carboxyl termini.
 AUTHOR: Jain S; Dolwick K M; Schmidt J V; Bradfield C A
 CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, Illinois 60611.
 CONTRACT NUMBER: ES05703 (NIEHS)
 T32 CA09560 (NCI)
 T32 ES07124 (NIEHS)
 SOURCE: Journal of biological chemistry, (1994 Dec 16) 269 (50) 31518-24.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199501
 ENTRY DATE: Entered STN: 19950124
 Last Updated on STN: 19950124
 Entered Medline: 19950112

AB The Ah **receptor** (AHR) is a ligand-activated transcription factor that is structurally related to its **dimerization** partner, the Ah **receptor nuclear** translocator (ARNT), and two Drosophila proteins, SIM and PER. All four proteins contain a region of homology now referred to as a PAS homology **domain**. In addition, the AHR, ARNT, and SIM harbor a basic region helix-loop-helix motif in their N termini, whereas PER does not. Previous mapping studies of the AHR have demonstrated that the PAS **domain** contains sequences required for ligand recognition, **dimerization**, and interaction with the 90-kDa heat shock protein. They also have confirmed that the basic region helix-loop-helix **domain** plays a role in both **dimerization** and sequence-specific DNA binding. To identify **domains** involved in transactivation of target genes, we generated **chimeras** of AHR/ARNT deletion mutants with the DNA binding region of the yeast Gal4 protein, transiently expressed these in COS-1 cells, . . . reporter gene under the control of a minimal promoter driven by enhancer elements recognized by Gal4. Extensive analysis of these **fusions** revealed that the AHR and ARNT harbor potent transactivation **domains** within their C termini. Importantly, the amino-terminal halves of both the AHR and ARNT were found to be devoid of. . .

L4 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 94022372 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 8415704
 TITLE: The PML-retinoic acid receptor alpha translocation converts the receptor from an inhibitor to a retinoic acid-dependent activator of transcription factor AP-1.
 AUTHOR: Doucas V; Brockes J P; Yaniv M; de The H; Dejean A
 CORPORATE SOURCE: Departement des Biotechnologies, Institut Pasteur, Paris, France.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 15) 90 (20) 9345-9. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931119

AB We report here that the **fusion** of PML, a **nuclear** protein defined by the t(15;17) chromosomal translocation in acute promyelocytic leukemia, with retinoic acid **receptor** alpha (RAR alpha) changes the RAR alpha from a retinoic acid (RA)-dependent inhibitor to a RA-dependent activator of AP-1 transcriptional activity. The PML-RAR alpha **chimera** cooperates with c-Jun and, strikingly, with c-Fos to stimulate the transcription of both synthetic and natural reporter genes containing an. . . a circumstance in which RAR alpha has no effect on AP-1 activity, PML-RAR alpha is an inhibitor. Deletion of the **dimerization**, transactivation, or DNA-binding **domains** of c-Jun and removal of the PML **dimerization domain** in the PML-RAR alpha hybrid abrogates their transcriptional cooperatively. In view of the association between AP-1 activity and hemopoietic differentiation,. . .

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L6 ANSWER 1 OF 10 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004065752 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14638687

TITLE: Contribution of the Per/Arnt/Sim (PAS) domains to DNA binding by the basic helix-loop-helix PAS transcriptional regulators.

AUTHOR: Chapman-Smith Anne; Lutwyche Jodi K; Whitelaw Murray L

CORPORATE SOURCE: School of Molecular and Biomedical Science (Biochemistry), University of Adelaide, South Australia, Australia.. anne.chapmansmith@adelaide.edu.au

SOURCE: Journal of biological chemistry, (2004 Feb 13) 279 (7) 5353-62. Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200403

ENTRY DATE: Entered STN: 20040210
Last Updated on STN: 20040331
Entered Medline: 20040330

AB . . . to stimuli such as hypoxia and environmental pollutants, mediated respectively by hypoxia inducible factors (HIF-alpha) and the dioxin (aryl hydrocarbon) **receptor** (DR). The bHLH proteins contain a basic DNA binding sequence adjacent to a helix-loop-helix **dimerization domain**. **Dimerization** among bHLH.PAS proteins is additionally regulated by the PAS region, which controls the specificity of partner choice such that HIF-alpha and DR must dimerize with the aryl hydrocarbon **nuclear** translocator (Arnt) to form functional DNA binding complexes. Here, we have analyzed purified bacterially expressed proteins encompassing the N-terminal bHLH and bHLH.PAS regions of Arnt, DR, and HIF-1alpha and evaluated the contribution of the PAS **domains** to DNA binding in vitro. Recovery of functional DNA binding proteins from bacteria was dramatically enhanced by coexpression of the. . . Arnt. Formation of stable protein-DNA complexes by DR/Arnt

and HIF-1alpha/Arnt heterodimers with their cognate DNA sequences required the PAS A **domains** and exhibited KD values of 0.4 nM and approximately 50 nM, respectively. In contrast, the presence of the PAS **domains** of Arnt had little effect on DNA binding by Arnt homodimers, and these bound DNA with a KD of 45. . . . In the case of the DR, both high affinity DNA binding and dimer stability were specific to its native PAS **domain**, since a **chimera** in which the PAS A **domain** was substituted with the equivalent **domain** of Arnt generated a destabilized protein that bound DNA poorly.

L6 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2002054090 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11677231
 TITLE: Determinants of subnuclear organization of mineralocorticoid receptor characterized through analysis of wild type and mutant receptors.
 AUTHOR: Pearce David; Naray-Fejes-Toth Aniko; Fejes-Toth Geza
 CORPORATE SOURCE: Division of Nephrology, Department of Medicine and Cellular & Molecular Pharmacology, University of California, San Francisco, California 94143, USA.. pearce@medicine.ucsf.edu
 CONTRACT NUMBER: DK51151 (NIDDK)
 DK54376 (NIDDK)
 DK55845 (NIDDK)
 SOURCE: Journal of biological chemistry, (2002 Jan 11) 277 (2) 1451-6.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200202
 ENTRY DATE: Entered STN: 20020125
 Last Updated on STN: 20030105
 Entered Medline: 20020207

AB The mineralocorticoid **receptor** (MR) is a hormone-dependent regulator of gene transcription that in the absence of ligand resides both in the cytoplasm and. . . MRs residing in the nucleus and cause aggregation of MRs into distinct clusters. To identify the functional determinants of MR **nuclear** organization, we examined the localization pattern of wild type MR and a series of mutants in the presence and absence of ligands using fluorescent protein **chimeras** in living cells. Our data show that although MR DNA binding is not necessary to mediate **nuclear** localization, it is absolutely required for wild type cluster formation as is an intact N-terminal or C-terminal activation function. In contrast, destabilization of a **dimerization** motif within the DNA-binding **domain** has no effect on subnuclear **receptor** architecture. These data suggest that normal MR cluster formation is dependent on both DNA binding and intact transcriptional activation functions but not on DNA-dependent **receptor dimerization**. Because dimer mutants bind with high affinity to hormone response element DNA multimers but not to single palindromic DNA sites, . . .

L6 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 2001378763 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11434903
 TITLE: Identification of a novel C-terminal domain involved in the negative function of the rainbow trout Ah receptor nuclear translocator protein isoform a (rtARNTa) in Ah receptor-mediated signaling.
 AUTHOR: Necela B; Pollenz R S
 CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, SC 29425, USA.
 CONTRACT NUMBER: ES 08980 (NIEHS)

SOURCE: Biochemical pharmacology, (2001 Aug 1) 62 (3) 307-18.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB Rainbow trout aryl hydrocarbon **receptor** (AHR) **nuclear** translocator isoform a (rtARNTa) has a negative function in AHR-mediated signal transduction. Previous analyses suggest that the negative function is. . . 57 C-terminal amino acids that are strongly hydrophobic. To assess the negative activity of rtARNTa at the molecular level, hydrophobic-rich **domains** corresponding to amino acids 601-637, 601-631, and 616-631 were analyzed for the ability to affect the function of truncated rtARNT proteins in complementation and gel shift assays. Addition of the hydrophobic-rich **domains** to these proteins reduced their ability to complement AHR-mediated signal transduction in mouse hepatoma cells by 65-95%. The decrease in. . . related to a reduced ability of the AHR. rtARNT complex to bind DNA and not due to a lack of **dimerization** with AHR. Expression of the hydrophobic-rich **domains** on Gal4 proteins showed that the C-terminal **domain** of rtARNTa was unlikely to contain transactivation function; however, the hydrophobic **domains** reduced the ability of the Gal4 proteins to bind DNA. Immunoprecipitation and mutational experiments indicate that the hydrophobic-rich **domains** do not interact with the bHLH motif of AHR. Interestingly, immunoprecipitation experiments also revealed that the C-terminal hydrophobic-rich region of rtARNTa could oligomerize in vitro in a **chimera** with the Gal4 DNA binding **domain**. These findings indicate that the C-terminal hydrophobic amino acids are critical for the negative function of rtARNTa in AHR-mediated signaling. . .

L6 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999182479 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10082558
TITLE: Design of conditionally active STATs: insights into STAT activation and gene regulatory function.
AUTHOR: Milocco L H; Haslam J A; Rosen J; Seidel H M
CORPORATE SOURCE: Ligand Pharmaceuticals Inc., San Diego, California 92121, USA.
SOURCE: Molecular and cellular biology, (1999 Apr) 19 (4) 2913-20.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990504
Last Updated on STN: 19990504
Entered Medline: 19990420

AB . . . biological role of STATs. To this end, we have developed a conditionally active STAT by fusing STATs with the ligand-binding **domain** of the estrogen **receptor** (ER). We have demonstrated that the resulting STAT-ER **chimeras** are estrogen-inducible transcription factors that retain the functional and biochemical characteristics of the cognate wild-type STATs. In addition, these tools have allowed us to evaluate separately the contribution of tyrosine phosphorylation and **dimerization** to STAT function. We have for the first time provided experimental data supporting the model that the only apparent role of STAT tyrosine phosphorylation is to drive **dimerization**, as **dimerization** alone is sufficient to

unmask a latent STAT **nuclear** localization sequence and induce **nuclear** translocation, sequence-specific DNA binding, and transcriptional activity.

L6 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998348380 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9685219
TITLE: Role of the conserved C-terminal region of thyroid hormone receptor-alpha in ligand-dependent transcriptional activation.
AUTHOR: Selmi-Ruby S; Casanova J; Malhotra S; Roussett B; Raaka B M; Samuels H H
CORPORATE SOURCE: Division of Molecular Endocrinology, Department of Medicine, New York University Medical Center, NY 10016, USA.
CONTRACT NUMBER: DK16636 (NIDDK)
SOURCE: Molecular and cellular endocrinology, (1998 Mar 16) 138 (1-2) 105-14.
JOURNAL code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981008
Last Updated on STN: 19981008
Entered Medline: 19980925

AB The ligand binding **domain** (LBD) of thyroid hormone (T3) **receptors** contains subdomains that participate in transcriptional activation, hormone-relieved repression and **dimerization**. A sequence conserved within the **nuclear receptor** superfamily is found at positions 397-405 of the 408-amino acid chicken T3 **receptor**-alpha (CTR alpha) and is deleted in the related avian v-erbA. Since v-erbA exhibits compromised ligand binding and transcriptional activation, this . . . reduced ligand-dependent transcriptional activity. The loss of transcriptional activity in CTR alpha(1-392) is not caused by impaired DNA binding or **receptor** dimer formation. Proteolytic protection assays reveal that both transcriptionally active and inactive CTR alpha derivatives undergo T3-mediated conformational changes. Gal4 **chimeras** containing the final 16, 35 or 44 amino acids of CTR alpha indicate that the conserved C-terminal region does not function as an independent transactivation **domain**. Our results are consistent with a model in which ligand plays a structural role to position the conserved C-terminal regions of CTR alpha and related **receptors** in a transcriptionally active conformation.

L6 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97294712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9148917
TITLE: Thyroid hormone-mediated enhancement of heterodimer formation between thyroid hormone receptor beta and retinoid X receptor.
AUTHOR: Collingwood T N; Butler A; Tone Y; Clifton-Bligh R J; Parker M G; Chatterjee V K
CORPORATE SOURCE: Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom.
SOURCE: Journal of biological chemistry, (1997 May 16) 272 (20) 13060-5.
JOURNAL code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970619

AB A subset of **nuclear receptors**, including those for thyroid hormone (TR), retinoic acid, vitamin D3, and eicosanoids, can form heterodimers with the retinoid X **receptor** (RXR) on DNA regulatory elements in the absence of their cognate ligands. In a mammalian two-hybrid assay, we have found that recruitment of a VP16-RXR **chimera** by a Gal4-TRbeta ligand-binding **domain** fusion is enhanced up to 50-fold by thyroid hormone (T3). This was also observed with a mutant fusion, Gal4-TR(L454A), lacking. . . in yeast. Hormone-dependent recruitment of RXR was also evident with another Gal4-TR mutant, AHTm, which does not interact with the **nuclear receptor** corepressor N-CoR, suggesting that ligand-enhanced **dimerization** is not a result of T3-induced corepressor release. Finally, we have shown that the interaction between RXR and TR is. . . effect. We propose that ligand-dependent heterodimerization of TR and RXR in solution may provide a further level of control in **nuclear receptor** signaling.

L6 ANSWER 7 OF 10 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97342635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9199332
TITLE: Heterodimeric interaction between retinoid X receptor alpha and orphan nuclear receptor OR1 reveals dimerization-induced activation as a novel mechanism of nuclear receptor activation.
AUTHOR: Wiebel F F; Gustafsson J A
CORPORATE SOURCE: Department of Biosciences at Novum, Karolinska Institute, Huddinge, Sweden.. franziska.wiebel@csb.ki.se
SOURCE: Molecular and cellular biology, (1997 Jul) 17 (7) 3977-86. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970724

AB OR1 is a member of the steroid/thyroid hormone **nuclear receptor** superfamily which has been described to mediate transcriptional responses to retinoids and oxysterols. On a DR4 response element, an OR1 heterodimer with the **nuclear receptor** retinoid X **receptor** alpha (RXR alpha) has been described to convey transcriptional activation in both the absence and presence of the RXR ligand. . . retinoic acid, the mechanisms of which have remained unclear. Here, we dissect the effects of RXR alpha and OR1 ligand-binding **domain** interaction on transcriptional regulation and the role of the respective carboxy-terminal activation **domains** (AF-2s) in the absence and presence of the RXR ligand, employing **chimeras** of the **nuclear receptors** containing the heterologous GAL4 DNA-binding **domain** as well as natural **receptors**. The results show that the interaction of the RXR and OR1 ligand-binding **domains** unleashes a transcription activation potential that is mainly dependent on the AF-2 of OR1, indicating that interaction with RXR activates OR1. This defines **dimerization**-induced activation as a novel function of heterodimeric interaction and mechanism of **receptor** activation not previously described for **nuclear receptors**. Moreover, we present evidence that activation of OR1 occurs by a conformational change induced upon heterodimerization with RXR.

L6 ANSWER 8 OF 10 MEDLINE on STN DUPLICATE 8
 ACCESSION NUMBER: 95295734 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7776971
 TITLE: Specificity of ligand-dependent androgen receptor stabilization: receptor domain interactions influence ligand dissociation and receptor stability.
 AUTHOR: Zhou Z X; Lane M V; Kemppainen J A; French F S; Wilson E M
 CORPORATE SOURCE: Department of Pediatrics, University of North Carolina, Chapel Hill 27599, USA.
 CONTRACT NUMBER: HD-04466 (NICHD)
 HD-16910 (NICHD)
 P30-HD-18968 (NICHD)
 SOURCE: Molecular endocrinology (Baltimore, Md.), (1995 Feb) 9 (2) 208-18.
 Journal code: 8801431. ISSN: 0888-8809.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199507
 ENTRY DATE: Entered STN: 19950720
 Last Updated on STN: 19970203
 Entered Medline: 19950710

AB . . . for the different physiological effects of testosterone (T) and dihydrotestosterone (DHT) was investigated using recombinantly expressed wild-type and mutant androgen **receptor** (AR). Rates of androgen dissociation from **nuclear** and cytoplasmic AR were compared with hormone- and concentration-dependent **receptor** degradation rates. T dissociates from AR 3 times faster than DHT or methyltrienolone (R1881) and is less effective in stabilizing the **receptor**. Analysis of AR deletion mutants and AR/glucocorticoid **receptor chimeras** indicates that the AR NH2-terminal **domain** has a specific role in stabilizing the **receptor** by slowing the rate of ligand dissociation and AR degradation. Amino acid mutations that abolish **receptor dimerization, nuclear** localization, or DNA-binding activity have no significant effect on androgen dissociation or AR degradation. A naturally occurring steroid-binding **domain** mutation (Val889 to Met) that causes androgen insensitivity, but does not alter equilibrium androgen binding affinity, lowered the androgen-binding capacity as a result of increased rates of androgen dissociation and AR degradation. Thus, AR stabilization and function require prolonged **receptor** occupancy with androgen, with a similar extent of stabilization observed at higher concentrations of faster dissociating androgens and lower concentrations of slower dissociating androgens. Retention of **receptor**-bound androgen is enhanced by an interaction between the AR NH2-terminal and steroid-binding **domains**. The ligand specificity and concentration dependence of **receptor** stabilization provide an explanation for physiological differences in the actions of T and DHT.

L6 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 9
 ACCESSION NUMBER: 95081092 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7989319
 TITLE: Potent transactivation domains of the Ah receptor and the Ah receptor nuclear translocator map to their carboxyl termini.
 AUTHOR: Jain S; Dolwick K M; Schmidt J V; Bradfield C A
 CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, Illinois 60611.
 CONTRACT NUMBER: ES05703 (NIEHS)
 T32 CA09560 (NCI)
 T32 ES07124 (NIEHS)
 SOURCE: Journal of biological chemistry, (1994 Dec 16) 269 (50)

31518-24.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950124
Last Updated on STN: 19950124
Entered Medline: 19950112

AB The Ah **receptor** (AHR) is a ligand-activated transcription factor that is structurally related to its **dimerization** partner, the Ah **receptor nuclear** translocator (ARNT), and two Drosophila proteins, SIM and PER. All four proteins contain a region of homology now referred to as a PAS homology **domain**. In addition, the AHR, ARNT, and SIM harbor a basic region helix-loop-helix motif in their N termini, whereas PER does not. Previous mapping studies of the AHR have demonstrated that the PAS **domain** contains sequences required for ligand recognition, **dimerization**, and interaction with the 90-kDa heat shock protein. They also have confirmed that the basic region helix-loop-helix **domain** plays a role in both **dimerization** and sequence-specific DNA binding. To identify **domains** involved in transactivation of target genes, we generated **chimeras** of AHR/ARNT deletion mutants with the DNA binding region of the yeast Gal4 protein, transiently expressed these in COS-1 cells, . . . by enhancer elements recognized by Gal4. Extensive analysis of these fusions revealed that the AHR and ARNT harbor potent transactivation **domains** within their C termini. Importantly, the amino-terminal halves of both the AHR and ARNT were found to be devoid of. . .

L6 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 94022372 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8415704

TITLE: The PML-retinoic acid receptor alpha translocation converts the receptor from an inhibitor to a retinoic acid-dependent activator of transcription factor AP-1.

AUTHOR: Doucas V; Brockes J P; Yaniv M; de The H; Dejean A

CORPORATE SOURCE: Departement des Biotechnologies, Institut Pasteur, Paris, France.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 15) 90 (20) 9345-9.
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 19940117

Last Updated on STN: 19940117

Entered Medline: 19931119

AB We report here that the fusion of PML, a **nuclear** protein defined by the t(15;17) chromosomal translocation in acute promyelocytic leukemia, with retinoic acid **receptor** alpha (RAR alpha) changes the RAR alpha from a retinoic acid (RA)-dependent inhibitor to a RA-dependent activator of AP-1 transcriptional activity. The PML-RAR alpha **chimera** cooperates with c-Jun and, strikingly, with c-Fos to stimulate the transcription of both synthetic and natural reporter genes containing an. . . a circumstance in which RAR alpha has no effect on AP-1 activity, PML-RAR alpha is an inhibitor. Deletion of the **dimerization**, transactivation, or DNA-binding **domains** of c-Jun and removal of the PML **dimerization domain** in the PML-RAR alpha hybrid abrogates their transcriptional cooperatively. In view of the association between AP-1 activity and hemopoietic differentiation,. . .